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Increased Heart Failure Hospitalization Rate in Smokers is Mediated by Preceding Ischemic Events in Patients With Heart Failure and Left Ventricular Dysfunction in SOLVD

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Background: Smoking has been demonstrated to increase rates of hospitalization due to heart failure (HF) in patients (pts) with heart failure or left ventricular dysfunction (LVD). Whether smoking exerts this effect through ischemic events has not been well established. **Methods:** We studied 6797 pts; 2569 pts in the Treatment Trial (T; LVD with HF) and 4228 pts in the Prevention Trial (P; LVD without HF) of the Studies of Left Ventricular Dysfunction (SOLVD). We evaluated hospitalization due to HF preceded by ischemic events (myocardial infarction or angina requiring hospitalization), over an average follow-up of 41.4 months in T and 37.4 months in P, comparing pts who were current smokers to non-smokers at baseline. Ischemic etiology accounted for 71% of HF pts in the T trial and 83% of LVD pts in the P trial. Current smokers accounted for 23% in the Combined Trials (T+P), 24% in the P Trial and 22% in the T Trial.

Results: After adjusting for age, gender, race, ejection fraction, atrial fibrillation, alcohol consumption, NYHA class, hypertension, diabetes mellitus, previous myocardial infarction, angina, etiology of left ventricular dysfunction, revascularization and medications, smokers had significantly higher hospitalization rates preceded by ischemic events in all pts in the Combined Trials (RR=1.59, p=0.003) and in the Prevention Trial (RR=1.86, p=0.005), and non-significantly higher hospitalization rate in the Treatment Trial (RR=1.39, p=0.14). Smoking did not significantly affect hospitalization rate for HF in patients that did not have preceding ischemic events.

Conclusion: The increase in hospitalization rate for heart failure in smokers in SOLVD is mediated by preceding ischemic events.

POSTER SESSION

1183 Transplant Allograft Vasculopathy

Tuesday, March 19, 2002, Noon-2:00 p.m.

Georgia World Congress Center, Hall G

Presentation Hour: Noon-1:00 p.m.

1183-147

Electron Beam Computed Tomography and Cardiac Transplant

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Background: Coronary allograft vasculopathy (CAV) is the leading cause of morbidity and mortality in cardiac transplant recipients surviving >1 year. Non-invasive diagnostic methods have generally been insensitive. Recently, electron beam computed tomography (EBCT) was suggested to have a high negative predictive value but the data are sparse.

Methods: 55 patients (13 female, 42 male) underwent coronary angiography and EBCT at a mean of 8 years after cardiac transplantation. The angiographic and EBCT data were reviewed separately in a blinded fashion. A coronary index score (CI) between 1 and 100 (100=normal) was calculated for each angiogram. The CI was derived using a combination of the BARI definitions and the National Heart and Chest Hospital algorithm. In these systems serial lesions multiply, parallel lesions add and vessels are weighted according to the amount of myocardium supplied. Individual lesions were rated according to length of artery wall involvement as well as luminal diameter narrowing. This method more accurately reflects the diffuse nature of CAV as opposed to focusing solely on severe stenoses. An EBCT score of >0 was considered abnormal.

Results: Twenty-seven patients had an EBCT score of zero. Thirty-six patients had a CI score of 100. Using the CI as the standard, EBCT resulted in 13 true positives, 14 false positives, 22 true negatives and 6 false negatives. The sensitivity of EBCT was 68%, the specificity was 61%. The disease prevalence was 35% so the accuracy was 64%. The positive predictive value of EBCT was 48% with a median EBCT score of 6.6 in the false positives and 70.5 in the true positives. The negative predictive value of EBCT was 79% with CI score ranging from 19-69 in the false negatives. These predictive values are substantially lower than in previous reports. Six patients had an EBCT score of zero despite having a mean CI score of 45. These patients were a median of 11 years post transplantation. Fourteen patients had a CI score of 100 despite having a median EBCT score of 10.7.

Conclusions: EBCT has low accuracy and predictive value for angiographic coronary artery disease in long-term cardiac transplant survivors.

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Shrinkage of Allograft Vessels Early After Transplantation Is Independent of Plaque Progression and Associated With Myocardial Fibrosis: A Serial Histologic and Volumetric Intravascular Ultrasound Study

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Shrinkage of allograft vessels has been described early after transplantation. The mechanisms are incompletely understood.

Methods: We examined 66 consecutive patients at 1 month and one year after transplantation with serial Intravascular Ultrasound (IVUS), using an automated pullback system (0.5mm/sec). Matched segments of the proximal LAD (average length 20mm) were identi-

fied. Using serial volumetric analysis (evenly spaced images 1mm apart), the lumen (L), vessel wall (EEM) and plaque (P=EEM-L) volumes were manually measured and average change in volumes was calculated. Serial endomyocardial biopsies during the first year of transplantation were examined for cellular rejection, vascular rejection, post transplant ischemia and fibrosis. Ischemic injury related to transplantation was identified by areas of myocyte necrosis occurring in the immediate post-transplant period with an absence of infiltration by activated lymphocytes. Interstitial myocardial fibrosis within a few weeks after transplantation, readily identified on H and E staining and after excluding scarring consistent with old biopsy site was considered consistent with ischemic-fibrotic injury.

Results: Expansion of vessel wall at one year was identified in 35/66 (53%) patients (Group A) and vessel wall shrinkage was seen in 31/66 (47%) patients (Group B). While patients in group A showed significant increase in average plaque volume, patients in group B showed no increase in plaque (1.14 Vs 0.15 mm³/mm, p=0.004). The incidence of post transplant myocardial ischemic-fibrotic injury was significantly higher in group B patients compared to group A (32% Vs 3%, p=0.001). There was no significant difference between the number of rejection episodes in the two groups.

Conclusion: In cardiac allograft vessels early shrinkage is independent of plaque progression and is associated with post transplant myocardial ischemic-fibrotic injury.

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Percutaneous Catheter Interventions for Cardiac Transplant Patients

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Background: Accelerated allograft arteriopathy limits the survival of patients who undergo orthotopic heart transplantation (OHT). Percutaneous catheter interventions (PCI) for stenoses in OHT patients was analyzed for the effect on graft survival and restenosis. **Methods:** The study included 103 coronary artery lesions from 50 interventional procedures in 35 patients who had OHT and were referred for PCI between July 1993-June 2001. The patients had yearly angiographic follow up for restenosis.

Results: The mean time after transplant was 6.2±3.3 yrs. The procedural success rate was 93%, defined as a post procedural lumen diameter stenosis <50% without a major complication. The baseline MLD was 0.6±0.6 mm and improved to 2.5±0.8 mm post procedure. The % diameter stenosis decreased from 79.8±19.3% at baseline to 13.0±15.4%. Coronary stenting was performed in 55 lesions (57%). Angiographic follow up in 57 lesions at 9.0±7.2 months showed a mean MLD of 1.4±1.2 mm, a % diameter stenosis of 49.4±40.5% and a restenosis rate of 44%. The allograft survival rate was 51% at 5 years after intervention (repeat OHT 9, death 3).

Conclusions: PCI can be an effective and safe method of treatment for allograft arteriopathy, or act as a temporizing measure until repeat OHT in patients with diffuse arteriopathy. The angiographic restenosis rate remains high, even in stented lesions.

Cardiac Transplant PCI	Stent	No Stent	p value
# of lesions	55	41	
Reference diameter (mm)	2.9±0.6	2.7±0.5	n.s.
Lesion length (mm)	14.9±7.4	14.7±6.7	n.s.
MLD (mm) before	0.7±0.6	0.4±0.5	p<0.05
after PCI	2.9±0.7	2.0±0.5	p<0.0001
Restenosis rate (%)	37	52	p=0.25

1183-150

Novel Noninvasive Strategy for Cardiac Allograft Vasculopathy Surveillance and Timing of Cardiac Catheterizations in Heart Transplant Recipients

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Background: With routine annual coronary angiography for transplant coronary artery disease (TxCAD) surveillance there are risks of major complications including renal failure because of chronic renal impairment due to cyclosporine. After promising results with regard to the noninvasive TxCAD diagnosis by electron beam computed tomography (EBCT) and pulsed tissue Doppler imaging (PW-TDI), we assessed the usefulness of a combined monitoring for TxCAD diagnosis using EBCT and PW-TDI together.

Methods: Throughout a testing period of 18 months, 196 heart recipients (post-transplant time: 1-16 years) underwent PW-TDI (for wall motion assessment) and EBCT (to detect coronary calcifications) before cardiac catheterization. With PW-TDI we measured the peak systolic and early diastolic wall motion velocities Sm and Em, the systolic and diastolic times TSm (from onset of the first heart sound to Sm) and TEm (from onset of the second heart sound to Em), as well as the systolic and early diastolic wall accelerations Sm/TSm and Em/TEm. Coronary calcifications were quantified by the Agatston scoring system. EBCT and PW-TDI data were tested for relationships with angiographic findings. **Results:** The systolic peak wall motion velocity (Sm) and the Agatston score (AS) showed high diagnostic values for TxCAD. We found highly significant differences (p=0.0001) between patients with and without proximal stenoses of the great epicardial coronary vessels for both the AS and Sm. Definite cut-off values for AS and Sm enabled highly diagnostic conclusions. The high negative predictive values for relevant coronary stenoses of Sm values below 9 cm/s (91.0%) and AS values below 50 (91.1%) allow coronary stenoses exclusion with high probability. Using both Sm and AS we obtained several functions that enable a diagnostic decision with similar probabilities of about 87 to 90%. Among these, Fisher's classification functions appeared most suitable for patient selection to coronary angiography on the base of PW-TDI and EBCT findings.

Conclusions: Serial PW-TDI and annual EBCT are reliable for timing of cardiac catheterizations and enable patients with high-risk for catheterization, to be spared routine angiographies.